

C L A I M S

1. Raloxifene acid addition salt or solvate thereof wherein the raloxifene acid addition salt of solvate thereof is selected among: raloxifene D-lactate, raloxifene L-lactate, Raloxifene DL-lactate, raloxifene D-lactate hemihydrate, raloxifene D-lactate $\frac{1}{4}$ -hydrate, raloxifene L-lactate hemihydrate, raloxifene L-lactate $\frac{1}{4}$ -hydrate, raloxifene DL-lactate hemihydrate and raloxifene DL-lactate $\frac{1}{4}$ -hydrate.

2. Raloxifene acid addition salt or solvate thereof according to claim 1, wherein the raloxifene acid addition salt or solvate thereof is raloxifene L-lactate hemihydrate being in crystalline form having the following X-ray crystalline positions:

XRD:

	D	2Theta	I(rel)	I(abs)	FWHM
15	14.639874	6.0322	17.56	6122	0.1200
	13.207421	6.6871	15.07	5254	0.1200
	10.875932	8.1229	80.41	28029	0.1200
20	9.268456	9.5347	22.67	7903	0.1200
	8.140638	10.8593	17.92	6247	0.1200
	7.488503	11.8083	15.59	5433	0.1000
	7.310331	12.0971	12.47	4347	0.0800
	7.089508	12.4754	25.79	8991	0.1000
25	6.931874	12.7603	12.78	4454	0.0900
	6.723932	13.1566	27.83	9701	0.1300
	6.551458	13.5045	14.20	4949	0.0900
	6.359432	13.9143	30.57	10656	0.1100
	6.130010	14.4378	21.33	7435	0.1300
30	5.853018	15.1249	36.40	12687	0.1100

	5.626204	15.7385	15.49	5401	0.1300
	5.507643	16.0795	23.25	8106	0.1000
	5.447238	16.2590	13.21	4606	0.0870
	5.224449	16.9573	19.21	6697	0.1100
5	5.160516	17.1690	17.10	5961	0.0870
	5.083475	17.4312	14.74	5137	0.1100
	4.954247	17.8896	19.64	6848	0.1000
	4.863750	18.2252	28.34	9879	0.0800
	4.805168	18.4494	46.26	16125	0.0700
10	4.756883	18.6383	49.99	17425	0.0800
	4.656926	19.0420	19.10	6659	0.1900
	4.630194	19.1530	17.96	6260	0.0870
	4.566015	19.4248	21.34	7438	0.1000
	4.487514	19.7680	12.76	4447	0.1000
15	4.347753	20.4101	11.69	4074	0.1100
	4.301465	20.6322	19.17	6682	0.0900
	4.224555	21.0120	14.55	5072	0.0870
	4.186561	21.2049	23.33	8134	0.1700
	4.065767	21.8425	26.06	9084	0.1000
20	4.015560	22.1190	17.10	5929	0.1000
	3.976949	22.3365	14.98	5223	0.0500
	3.935785	22.5732	34.50	12028	0.1100
	3.867038	22.9799	100.00	34859	0.1000
	3.779481	23.5198	40.14	13991	0.0800
25	3.742319	23.7567	59.68	20805	0.1000
	3.710418	23.9640	13.17	4591	0.0870
	3.645564	24.3968	11.19	3902	0.0800
	3.621808	24.5593	18.71	6524	0.1000
	3.552536	25.0459	16.01	5581	0.1000
30	3.516088	25.3098	13.46	4691	0.0600

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	3.498357	25.4402	12.66	4413	0.0700
	3.467075	25.6737	10.74	3745	0.0500
	3.418947	26.0414	21.49	7491	0.1000
	3.395298	26.2260	12.12	4225	0.0870
5	3.369948	26.4268	15.48	5369	0.0700
	3.358554	26.5181	14.33	4995	0.0600
	3.244985	27.4641	11.90	4149	0.0700
	3.229427	27.5990	9.63	3356	0.0870
	3.177657	28.0578	15.07	5253	0.1200
10	3.144884	28.3562	32.65	11381	0.1000
	3.106130	28.7176	9.83	3425	0.0800
	3.082970	28.9380	9.00	3138	0.0870
	3.056106	29.1980	8.56	2984	0.0870
	3.032184	29.4335	8.74	3048	0.1100
15	2.994539	29.8121	8.27	2884	0.0700
	2.979114	29.9700	9.26	3229	0.0800
	2.924922	30.5387	9.19	3203	0.1800
	2.870290	31.1346	16.32	5689	0.1400
	2.828902	31.6019	13.59	4737	0.1100
20	2.762611	32.3808	10.83	3775	0.1000

3. Raloxifene acid addition salt or solvate thereof according to claim 1,
 wherein the raloxifene acid addition salt or solvate thereof is raloxifene L-lactate
 ¼-hydrate being in crystalline form having the following X-ray crystalline posi-
 25 tions:

XRD:

<u>D</u>	<u>2Theta</u>	<u>I(rel)</u>	<u>I(abs)</u>	<u>FWHM</u>
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	14.079244	6.2726	45.93	16568	0.1300
	9.974912	8.8580	32.43	11699	0.1100
	9.526523	9.2758	71.31	25721	0.1200
	8.215598	10.7600	47.82	17248	0.1100
5	7.246270	12.2045	80.04	28871	0.1100
	7.065557	12.5178	16.17	5832	0.0700
	6.878001	12.8606	22.74	8201	0.1200
	6.283709	14.0828	66.27	23901	0.0800
	6.194698	14.2862	53.98	19470	0.0984
10	5.859529	15.1080	11.17	4028	0.0984
	5.744935	15.4112	16.16	5828	0.1200
	5.312222	16.6751	18.02	6499	0.1200
	5.046910	17.5585	34.26	12356	0.0900
	4.978933	17.8001	54.66	19715	0.1000
15	4.918535	18.0205	17.40	6277	0.0984
	4.746264	18.6804	26.77	9655	0.1000
	4.712771	18.8143	46.35	16716	0.0900
	4.569429	19.4101	57.60	20777	0.1000
	4.455985	19.9093	53.60	19332	0.1200
20	4.345589	20.4204	12.70	4579	0.0900
	4.268096	20.7952	86.33	31139	0.0900
	4.106332	21.6241	20.17	7274	0.1100
	4.042283	21.9710	22.73	8197	0.1200
	3.944656	22.5218	23.46	8462	0.1000
25	3.913129	22.7056	100.00	36069	0.1100
	3.831706	23.1947	15.49	5586	0.0900
	3.777075	23.5350	69.72	25148	0.1400
	3.735872	23.7983	14.85	5358	0.0984
	3.667856	24.2463	11.94	4305	0.0900
30	3.639035	24.4413	13.87	5001	0.0800

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	3.589918	24.7809	9.38	3383	0.0984
	3.545715	25.0949	23.58	8505	0.0800
	3.505655	25.3864	33.63	12131	0.1100
	3.442223	25.8622	22.60	8152	0.1100
5	3.411017	26.1030	10.82	3901	0.0984
	3.371851	26.4117	44.16	5108	0.1000
	3.280618	27.1600	15.23	5494	0.1100
	3.251104	27.4114	14.23	5134	0.0800
	3.232072	27.5760	19.25	6943	0.1100
10	3.153056	28.2812	12.42	4479	0.1900
	3.143130	28.3724	12.29	4432	0.0984
	3.081939	28.9479	17.16	6189	0.2200
	3.040378	29.3524	9.73	3510	0.1300
	2.990508	29.8532	15.29	5514	0.1400
15	2.929711	30.4876	11.37	4102	0.1200
	2.892397	30.8906	18.91	6822	0.1200
	2.856192	31.2922	8.91	3214	0.1100
	2.818108	31.7261	14.79	5336	0.2500
	2.765584	32.3450	15.86	5720	0.1300

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4. Raloxifene acid addition salt or solvate thereof according to claim 1, wherein the raloxifene acid addition salt or solvate thereof is raloxifene DL-lactate hemihydrate being in crystalline form having the following X-ray crystalline positions:

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XRD:

	<u>D</u>	<u>2Theta</u>	<u>I(rel)</u>	<u>I(abs)</u>	<u>FWHM</u>
30	13.595814	6.4959	28.40	12683	0.1400

	10.855533	8.1382	16.15	7211	0.1200
	9.849394	8.9711	32.17	14369	0.1000
	9.534325	9.2682	66.95	29898	0.1300
	8.150249	10.8465	45.20	20188	0.1300
5	7.240730	12.2138	63.53	28374	0.1400
	6.769843	13.0670	18.42	8227	0.1500
	6.272666	14.1077	75.67	33794	0.1900
	5.818832	15.2143	13.28	5933	0.2000
	5.657337	15.6513	18.07	8070	0.1300
10	5.505030	16.0872	10.51	4692	0.1000
	5.261933	16.8357	17.48	7806	0.1400
	5.089504	17.4104	16.14	7210	0.1000
	5.001569	17.7189	41.94	18732	0.0900
	4.958950	17.8725	29.16	13023	0.1148
15	4.797388	18.4795	19.39	8660	0.1100
	4.669322	18.9910	49.20	21972	0.1400
	4.574684	19.3876	63.21	28227	0.1000
	4.533019	19.5676	44.94	20071	0.1148
	4.440548	19.9792	32.70	14604	0.1200
20	4.301886	20.6301	100.00	44659	0.1500
	4.155406	21.3657	78.00	34833	0.1600
	4.059049	21.8797	27.53	12296	0.1800
	3.960846	22.4285	25.59	11427	0.1000
	3.907408	22.7393	83.48	37282	0.1200
25	3.865461	22.9894	16.46	7350	0.1148
	3.828892	23.2120	17.46	7798	0.0900
	3.773130	23.5599	50.71	22649	0.1200
	3.716486	23.9243	23.06	10300	0.1300
	3.652238	24.3515	15.79	7053	0.1800
30	3.584725	24.8174	12.91	5764	0.1500

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	3.486791	25.5261	30.45	13600	0.1200
	3.439149	25.8858	22.21	9919	0.1300
	3.396267	26.2184	17.86	7978	0.1100
	3.370045	26.4261	12.48	5572	0.1148
5	3.329320	26.7553	9.21	4113	0.1100
	3.292728	27.0582	11.81	5274	0.1000
	3.278070	27.1815	11.25	5026	0.1148
	3.218620	27.6935	21.24	9485	0.1900
	3.167986	28.1452	13.80	6162	0.0900
10	3.143230	28.3715	30.33	13546	0.1000
	3.095423	28.9191	14.02	6260	0.1200
	3.024921	29.5058	11.56	5161	0.1400
	3.007253	29.6831	13.40	5984	0.1300

- 15 5. Raloxifene acid addition salt or solvate thereof being raloxifene succinate in crystalline form having the following X-ray crystallographic positions:

XRD:

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	D	2Theta	I(rel)	I(abs)	FWHM
	13.195230	6.6933	20.78	8475	0.1400
	9.695642	9.1137	13.43	5476	0.0300
25	9.304945	9.4972	18.19	7419	0.1300
	8.394523	10.5300	13.26	5407	0.1000
	7.944460	11.1283	14.15	5768	0.1000
	7.708667	11.4699	17.61	7180	0.1200
	7.526675	11.7482	12.32	5023	0.0898
30	7.323294	12.0756	15.22	6205	0.1000

	7.160495	12.3512	13.04	5316	0.0800
	6.926815	12.7696	23.68	9655	0.1300
	6.606409	13.3917	29.08	11856	0.1400
	6.463392	13.3894	14.45	5891	0.0898
5	6.285432	14.0789	21.24	8662	0.1200
	6.127742	14.4432	63.63	25947	0.1200
	5.961999	14.8469	15.55	6342	0.0900
	5.875574	15.0665	15.77	6430	0.0898
	5.788967	15.2933	16.15	6585	0.1400
10	5.624221	15.7441	34.74	14167	0.1200
	5.453763	16.2394	22.89	9334	0.1300
	5.276560	16.7887	12.71	5182	0.1200
	5.095057	17.3913	14.19	5786	0.1100
	5.020392	17.6520	11.12	4535	0.0898
15	4.835944	18.3309	18.30	7461	0.1200
	4.765096	18.6059	18.62	7591	0.1100
	4.630456	19.1519	65.88	26864	0.1600
	4.525518	19.6003	15.16	6180	0.0800
	4.484997	19.7792	24.48	9982	0.1000
20	4.376528	20.2745	18.78	7659	0.1000
	4.352225	20.3889	19.11	7790	0.1000
	4.227757	20.9959	29.39	11984	0.1000
	4.191265	21.1808	56.82	23171	0.0800
	4.158052	21.3520	40.16	16377	0.0898
25	4.101947	21.6475	17.14	6988	0.0800
	4.062068	21.8626	19.79	8072	0.1000
	4.010082	22.1496	11.70	4771	0.0600
	3.921660	22.6556	100.00	40776	0.1300
	3.860487	23.0194	29.04	11842	0.1100
30	3.813566	23.3066	19.25	7850	0.1100

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	3.732687	23.8189	19.33	7884	0.1300
	3.694791	24.0669	22.47	9161	0.1100
	3.644300	24.4054	18.84	7680	0.1400
	3.544078	25.1067	13.63	5556	0.0700
5	3.496160	25.4565	16.28	6637	0.0898
	3.446458	25.8299	20.36	8300	0.2100
	3.398344	26.2021	12.35	5036	0.1200
	3.373032	26.4022	8.82	3597	0.0898
	3.305938	26.9481	14.08	5741	0.1100
10	3.281940	27.1489	10.08	4112	0.0898
	3.260437	27.3314	9.66	3937	0.0898
	3.227083	27.6194	19.22	7838	0.1200
	3.179256	28.0434	16.28	6640	0.2600
	3.146269	28.3435	8.89	3627	0.0898
15	3.121159	28.5764	9.58	3907	0.0900
	3.097691	28.7975	10.64	4337	0.0400
	3.074307	29.0213	19.64	8008	0.1200
	3.032262	29.4328	10.17	4148	0.1300
	3.010128	29.6541	9.43	3847	0.0898

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6. Raloxifene acid addition salt or solvate thereof being raloxifene sulphate 2-propanol solvate.

7. Raloxifene acid addition salt or solvate thereof according to claim 6, wherein raloxifene sulphate 2-propanol solvate is in crystalline form having the following X-ray crystallographic positions:

XRD:

<u>D</u>	<u>2Theta</u>	<u>I(rel)</u>	<u>I(abs)</u>	<u>FWHM</u>
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	14.374007	6.1439	26.57	5009	0.0900
	10.303750	8.5748	29.62	5583	0.1300
	9.201529	9.6042	26.22	4942	0.1100
	8.871726	9.9621	29.84	5624	0.1300
5	8.569965	10.3138	22.25	4195	0.0400
	8.320378	10.6241	25.97	4896	0.1200
	7.945119	11.1274	38.65	7286	0.1300
	7.514174	11.7678	20.56	3876	0.1041
	7.205108	12.2745	25.04	4721	0.1400
10	6.537437	13.5336	66.78	12590	0.1400
	6.228787	14.2076	21.88	4126	0.1100
	5.628329	15.7325	20.71	3904	0.0900
	5.540447	15.9837	27.40	5166	0.1100
	5.322476	16.5489	64.98	12249	0.1500
15	5.138694	17.2425	21.65	4082	0.1100
	5.020317	17.6522	64.05	12074	0.1400
	4.706881	18.8381	100.00	18851	0.1300
	4.618097	19.2036	60.47	11400	0.0800
	4.538129	19.5453	59.35	11189	0.1100
20	4.471816	19.8381	67.03	12636	0.1200
	4.261964	20.8255	54.78	10327	0.1100
	4.204757	21.1121	51.35	9680	0.1600
	4.156029	21.3625	46.65	8794	0.1041
	4.093305	21.6938	25.93	4888	0.0900
25	4.035960	22.0058	24.21	4563	0.1800
	3.937182	22.5651	25.37	4784	0.1200
	3.835400	23.1721	22.17	4179	0.0900
	3.796528	23.4127	40.94	7718	0.0900
	3.767170	23.5978	61.03	11505	0.1100
30	3.691303	24.0899	20.10	3790	0.1500

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	3.639317	24.4393	47.20	8897	0.1200
	3.590489	24.7769	28.23	5321	0.1600
	3.511060	25.3467	29.66	5592	0.1100
	3.478586	25.5873	23.70	4468	0.1041
5	3.416539	26.0601	37.38	7047	0.1900
	3.355389	26.5436	20.28	3823	0.1300
	3.314637	26.8760	17.08	3220	0.1200
	3.271015	27.2413	15.24	2874	0.0600
	3.252583	27.3987	14.71	2773	0.1041
10	3.100446	28.7714	23.04	4344	0.1200
	3.079703	28.9694	19.73	3720	0.1041
	3.033828	29.4172	29.23	5511	0.1300
	3.009744	29.6580	15.28	2880	0.1041
	2.937725	30.4024	13.30	2507	0.1700

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8. Raloxifene acid addition salt or solvate thereof being raloxifene malonate in crystalline form having the following X-ray crystalline positions:

XRD:

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	<u>D</u>	<u>2Theta</u>	<u>I(rel)</u>	<u>I(abs)</u>	<u>FWHM</u>
	14.385166	6.1391	36.51	6471	0.0100
	13.125024	6.7292	38.91	6896	0.1300
25	10.305386	8.5734	37.32	6614	0.1700
	9.279238	9.5236	39.85	7062	0.1300
	8.860721	9.9745	34.60	6133	0.0900
	8.510328	10.3863	33.27	5895	0.0900
	8.314361	10.6318	33.02	5852	0.0800
30	7.947949	11.1234	41.61	7375	0.1600

	7.265135	12.1727	35.79	6343	0.1300
	6.882996	12.8512	29.65	5254	0.0300
	6.537915	13.5326	60.19	10667	0.1800
	6.258251	14.1404	61.12	10833	0.2100
5	6.003203	14.7444	31.92	5657	0.1200
	5.877911	15.0605	29.17	5170	0.0600
	5.794580	15.2784	29.33	5198	0.0200
	5.663226	15.6349	49.63	8796	0.1300
	5.550457	15.9547	36.61	6487	0.0800
10	5.354103	16.5438	55.84	9897	0.2200
	5.134028	17.2583	30.18	5349	0.1378
	5.023848	17.6397	55.21	9784	0.2100
	4.836637	18.3283	36.13	6404	0.1400
	4.700761	18.8628	71.64	12696	0.1600
15	4.644808	19.0922	86.46	15323	0.1500
	4.538522	19.5436	61.36	10874	0.1300
	4.472256	19.8361	50.40	8931	0.1000
	4.347111	20.4132	37.86	6709	0.1000
	4.247918	20.8951	88.12	15616	0.2300
20	4.161428	21.3344	73.93	13101	0.1600
	4.085803	21.7341	37.19	6591	0.1100
	4.019584	22.0966	35.60	6309	0.1500
	3.921695	22.6554	100.00	17722	0.1700
	3.765729	23.6059	50.70	8986	0.2000
25	3.703455	24.0097	34.79	6166	0.1200
	3.638542	24.4446	47.30	8382	0.1900
	3.499221	25.4339	44.29	7849	0.2000
	3.426872	25.9801	43.63	7732	0.2200
	3.292398	27.0610	23.39	4145	0.1000
30	3.253755	27.3886	25.03	4435	0.1400

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3.192249	27.9269	22.18	3931	0.1400
3.094846	28.8246	28.68	5083	0.3000
3.034329	29.4123	27.30	4338	0.1900

5 9. Use of a raloxifene acid addition salt or solvate thereof according to any of the claims 1-8, for the manufacture of a pharmaceutical composition capable of fast and reliable release of the raloxifene acid addition salt or solvate thereof in gastric juice.

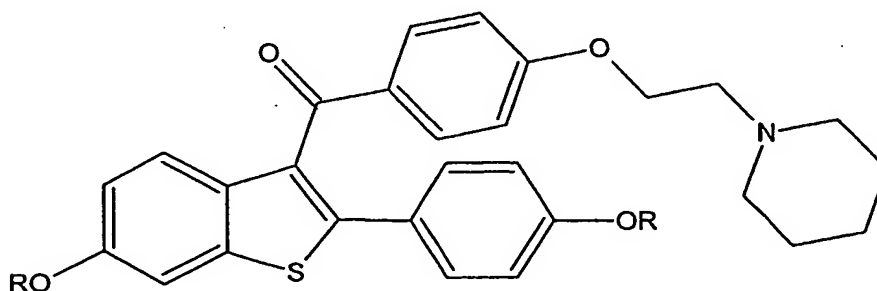
10 10. Use according to claim 9, where the pharmaceutical composition is intended for the treatment of cancer or osteoporosis, or for inhibiting cartilage degradation.

11. Pharmaceutical composition capable of fast and reliable release of the active ingredients in gastric juice, comprising a raloxifene acid addition salt or solvate thereof according to any of the claims 1-8.

15 12. Pharmaceutical composition according to claim 11, wherein the pharmaceutical is intended for the treatment of cancer or osteoporosis, or for inhibiting cartilage degradation.

13. Process for the manufacture of raloxifene lactate comprising the following steps:

20 to a solution of the compound having the general formula I in an solvent



Formula I

25

wherein R represents two independently selected hydroxyl protec-

tion groups,

a suitable reagent is added in order to remove the protection groups;

lactic acid is added to the mixture, and

raloxifene lactate is precipitated from the mixture and isolated.

- 5 14. Process according to claim 13, wherein the groups R are independently selected from: C₁-C₄ alkyl, C₅-C₇ cycloalkyl, benzyl -COR² or SO₂R², wherein R² is C₁-C₄ primary or secondary alkyl, C₁-C₃ fluoroalkyl, C₁-C₃ chloroalkyl, C₁-C₄ alkylphenyl, C₁-C₄ alkoxyphenyl, mono- or dinitrophenyl or mono- or di(chloro or fluoro)phenyl.

- 10 15. Process according to the claims 13 or 14, wherein the two R groups are identical.

16. Process according to the claims 13-15, wherein the solvent is selected from alcohols having 1 to 5 carbon atoms.

- 15 17. Process according to claim 16, wherein the alcohol is a monovalent alcohol.

18. Process according to claim 17, wherein the alcohol is ethanol.

19. Process according to claim 18, wherein the alcohol is 96% ethanol.

20. Process according to any of the claims 13 to 19, wherein the lactate is L-lactate.